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BRIDGING THE GAP: INOTUZUMAB INTEGRATION PRIOR TO TALICABTAGENE AUTOLEUCEL IN R/R B-ALL

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INTRODUCTION

- **Tali-cel (Talicabatgene autoleucel)** is a CD19 CAR-T cell product showing promise in relapsed/refractory (r/r) B-ALL.(1)
- Disease burden at infusion impacts long-term efficacy and safety.
- **Inotuzumab ozogamicin** is a CD22-directed antibody-drug conjugate effective in reducing disease burden.(2)
- Concerns include **hepatotoxicity** and potential interference with **CAR-T expansion**.(2)

AIM

To evaluate the **safety, efficacy, and feasibility** of inotuzumab-based regimens prior to Tali-cel infusion in r/r B-ALL patients.
Improve CAR-T outcomes without consolidative allogeneic stem-cell transplant (alloSCT).

METHOD

Study Design
This was a **retrospective analysis** conducted at **Tata Memorial Hospital, Mumbai** between **November 2023 and January 2025**. The study included patients aged **≥15 years** with **relapsed/refractory B-cell acute lymphoblastic leukemia (r/r B-ALL)** who were registered to receive **Tali-cel**, a CD19-directed CAR-T cell therapy, as part of the institutional standard-of-care protocol.

Subgroup Focus
Patients who received **inotuzumab ozogamicin** as **salvage or bridging therapy** prior to Tali-cel infusion were further evaluated:
- Baseline disease characteristics
- Inotuzumab treatment specifics (dose, timing, response, toxicities)
- CAR-T dose and administration
- Post-CAR-T response and toxicities
- **B-cell aplasia** duration as a surrogate for CAR-T persistence

Definitions & Response Criteria
- **Response Assessment**: Based on **ELN 2024** criteria
- **Minimal Residual Disease (MRD)**: Evaluated using **10-color flow cytometry**, with a sensitivity of **10^{-4}** cells
- **Toxicity Grading**:
  - **CRS, ICANS, IEC-HS**: Graded per **ASTCT consensus criteria**
  - **Other adverse events**: Graded using **CTCAE version 5**

Statistical Analysis
- **Descriptive statistics** were used to summarize:
  - Baseline characteristics
  - Treatment responses
  - Toxicity profiles
- **Survival analysis**:
  - Performed using the **Kaplan–Meier method**
  - Key endpoints: **Overall survival (OS)** and **Event-free survival (EFS)**

RESULTS

Out of 73 patients with B-ALL registered for tali-cel therapy, 56 (77%) underwent apheresis and 46 (63%) received the CAR-T cell infusion. Inotuzumab-based regimens were used in 32 patients (44%), primarily as salvage (31%), bridging (25%), or both (44%). Among these, 78% (25/32) proceeded to receive tali-cel infusion.
At the time of tali-cel infusion, the disease burden was significantly reduced:
- **Baseline median disease burden**: 3% (range: 0–96%)
- **At infusion**: 2% (range: 1–74%)

The median cumulative dose of inotuzumab administered before infusion was **0.6 mg/m²** (range: 0.3–3.0), with the **last dose given a median of 26 days** (range: 17–86) before infusion. Mini-Hyper CVD was the most common concurrent chemotherapy, used in 66% (21/32) of inotuzumab-treated patients.
In Philadelphia chromosome-positive (Ph+) ALL (n = 9), tyrosine kinase inhibitors were permitted:
- **Ponatinib**: 80% (4/5)
- **Dasatinib**: 20% (1/5)

Pre-Infusion Assessment (n = 25)
- **Complete response (CR)**: 84% (21/25)
- **MRD clearance**: 64% (16/25)

Post-Tali-cel Infusion Outcomes (n = 25)
- **CR after infusion**: 88% (22/25)
- **MRD negative after infusion**: 88% (22/25)
- **Median follow-up**: 6 months (range: 1–11 months)
- **6-month overall survival (OS)**: 84%
- **6-month progression-free survival (PFS)**: 80%
- **Median OS/PFS**: Not reached
- **No patients underwent allogeneic stem cell transplantation (allo-SCT)** as consolidation

Tali-cel therapy was generally well tolerated, although infections and immune-related toxicities were common:
Adverse Events (Grade 3–4)
- **Infections**: 76% (19/25)
- **Hepatotoxicity**: 4% (1/25)
- **CRS (Cytokine Release Syndrome)**: 4% (1/25)
- **ICANS (Immune effector cell-associated neurotoxicity syndrome)**: 4% (1/25)
- **IEC-HS (Immune effector cell–associated hemophagocytic syndrome)**: 36% (9/25)

In exploratory analysis, **persistent B-cell aplasia** was observed in **76% (19/25)** of patients at the last follow-up, suggesting ongoing CAR-T activity.

Table no 1: Summary of Results

Age (years)	**Median: 22 (Range: 16–64)**
Gender	Male: 75% (24/32), Female: 25% (8/32)
Previous Lines of Therapy	Median: 2 (Range: 1–5)
Blast % at Baseline	Median: 3% (Range: 0–96)
Blast % at Time of Infusion	Median: 2% (Range: 1–74)
Ph+ ALL	28% (9/32)
CR to Bridging (n=25 infused)	84% (21/25)
MRD Clearance (n=25 infused)	64% (16/25)
Toxicities (Post-Tali-cel Infusion)	
CRS (Grade 3/4)	4% (1/25)
ICANS (Grade 3/4)	4% (1/25)
IEC-HS (Grade 3/4)	36% (9/25)
Hepatotoxicity (3/4)	4% (1/25)
Infections	76% (19/25)
B-cell Aplasia	76% (19/25)

CONCLUSIONS

- Inotuzumab-based regimens, including as salvage/bridging, were feasible before Tali-cel infusion.
- High CR and MRD clearance rates were observed pre- and post-infusion.
- Toxicities were manageable, with low rates of severe CRS/ICANS.
- No patients proceeded to allo-SCT, yet outcomes at 6 months were favorable.
- Further follow-up is needed to determine durability of responses and long-term safety

REFERENCES

1 Jain H, Karulkar A, Kalra D, Ravikumar S, Shah S, Firfiray A *et al.* Talicabtagene autoleucel for relapsed or refractory B-cell malignancies: results from an open-label, multicentre, phase 1/2 study. *Lancet Haematol* 2025; 12: e282–e293.
2 Rheingold SR, Ji L, Gore L, Xu X, Bhojwani D, Shah NN *et al.* Impact of Treatment with Inotuzumab Ozogamicin before or after Chimeric Antigen Receptor T-Cell Therapy in Children with Relapsed/Refractory Acute Lymphoblastic Leukemia. *Blood* 2023; 142: 2876–2876.

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